

## High tumor burden in non-small cell lung cancer: review of the literature

Luis Cabezón-Gutiérrez\*, María Sereno, Raquel Cervera-Calero, Xabier Mielgo-Rubio,  
Oliver Higuera

\*Corresponding author:

Luis Cabezón-Gutiérrez

*Medical Oncology, Hospital Universitario de Torrejón, C/Mateo Inurria N°1, CP 28850,  
Torrejón de Ardoz (Madrid). España*

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Handling editor:

Michal Heger

*Department of Pharmaceutics, Utrecht University, the Netherlands*

*Department of Pharmaceutics, Jiaxing University Medical College, Zhejiang, China*

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1<sup>st</sup> Editorial decision  
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Ref.: Ms. No. JCTRes-D-22-00051

High Tumor burden in non-small cell lung cancer. Review of the literature.  
Journal of Clinical and Translational Research

Dear Dr Cabezón-Gutiérrez,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

Please note that the reviewer recommended to reject the paper. The editorial board has considered the reviewer's comments and weighed these against the probability of resolving the reviewer's concern. Consequently, we would like to give the authors a chance at conducting a deep dive on their manuscript and modifying the paper accordingly.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that

the track changes function is switched on when implementing the revisions.  
This enables the reviewers to rapidly verify all changes made.

Your revision is due by Aug 04, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The authors tried to explain the concept of TB as well as the relationship between the NSCLC, TB, and response to treatment by summarizing the existing relevant literature. It is an interesting but not innovative topic. And I still can't get a relative definite conclusion from reading the whole article. Besides, the authors did not make their own summary and reflection on the relevant literature. I do not recommend that this manuscript be published on Journal of Clinical and Translational Research. Some other suggestions were listed below.

1.It is not advised that "predictive biomarker and immunotherapy" to be a keyword in this article as it concluded two important concepts.

2.In methods part, authors describe "the keywords included non-small cell lung cancer, tumor burden, aggressive disease, prognosis biomarker, predictive biomarker and immunotherapy", however, the topic of this review of the literature should be the association between TB and NSCLC according to the tittle, thus immunotherapy should not be a keyword in literature search.

3.A flowchart describing the processing of non-systematic literature review was advised as I am not sure how many RCTs or retrospective studies and case series were included.

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Authors' response

**Response to reviewers:**

1.It is not advised that "predictive biomarker and immunotherapy" to be a keyword in this article as it concluded two important concepts. **We have removed the words predictive and prognostic biomarkers and immunotherapy from the keywords according to the reviewer's suggestion.**

2. In methods part, authors describe "the keywords included non-small cell lung cancer, tumor burden, aggressive disease, prognosis biomarker, predictive biomarker and immunotherapy",

however, the topic of this review of the literature should be the association between TB and NSCLC according to the title, thus immunotherapy should not be a keyword in literature search. **We have removed the word immunotherapy from the keywords and literature search according to the reviewer's suggestion.**

3. A flowchart describing the processing of non-systematic literature review was advised as I am not sure how many RCTs or retrospective studies and case series were included.

**We have added a paragraph on the search criteria and number of articles found, clarifying that it is a review but not a systematic one that includes other articles that qualify the concept of high tumor burden (it is very difficult to find such a term in the title/abstract of the articles), being a concept widely used in routine clinical practice but without a clear definition or description in the literature, hence the interest of the current manuscript).**

4. The authors tried to explain the concept of TB as well as the relationship between the NSCLC, TB, and response to treatment by summarizing the existing relevant literature. It is an interesting but not innovative topic. And I still can't get a relative definite conclusion from reading the whole article. Besides, the authors did not make their own summary and reflection on the relevant literature. **We have added a paragraph in the conclusions section about what in our opinion is considered a high tumor burden based on what is developed in the text, as suggested by the reviewer.**

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2<sup>nd</sup> Editorial decision  
27-Aug-2022

Ref.: Ms. No. JCTRes-D-22-00051R1  
High Tumor burden in non-small cell lung cancer. Review of the literature.  
Journal of Clinical and Translational Research

Dear Dr Cabezón-Gutiérrez,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended as a separate file to this email. Please continue any revision using the appended file instead of the revision you had uploaded.

If you decide to revise the work, please submit a list of changes or a rebuttal against each

point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Aug 26, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #2: Dear authors,

Thank you for revising the draft according to the reviewer's comments.

I have carefully gone through the revision and made corrections at numerous locations. Please see the draft attached. I urge you to continue any modifications in the draft appended to this decision email.

Furthermore, there are several key points that still need to be addressed before we can proceed to considering acceptance of the paper.

- 1) The manuscript needs to be proofread by a native speaker. I do not have the time to do everything for you (it is also not my responsibility).
- 2) There are many abbreviations that were not written out in full at first mention. Please correct this. Also, eliminate abbreviations that are used 2 or 3 times in the entire paper. In those instances, just write it out in full to not overcomplicate the manuscript.
- 3) One of the most important critiques by the previous reviewer as well as myself is that your text is not argumentative. There are no reasons provided for why a certain marker or parameter for high tumor burden should or should not be included in the set of parameters through which high tumor burden is defined. There is no logical pretext for your definition and conclusions, merely a narrative summary of findings in other people's work. In other words, what is the justification for choosing "more than 3 metastatic sites, the sum of the longest diameters larger than 100 mm, metastatic liver involvement, multiple symptomatic brain involvement, and relevant functional patient deterioration" as criteria for HTB? This needs to be overly evident and premised in the preceding text.

Once you have addressed these aspects, please resubmit your revision and we will see whether the criteria for acceptance are met in a final review round.

Please understand that it will take a considerable overhaul on your part to get this manuscript on the right track. Do not take my comments lightly, please.

Thank you and good luck,

Michal Heger  
Editor

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

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Authors' response

**Response to reviewer:**

- 1) The manuscript needs to be proofread by a native speaker. I do not have the time to do everything for you (it is also not my responsibility). **Some of the text has been revised and modified by a native speaker.**
  - 2) There are many abbreviations that were not written out in full at first mention. Please correct this. Also, eliminate abbreviations that are used 2 or 3 times in the entire paper. In those instances, just write it out in full to not overcomplicate the manuscript. **Modifications have been made as suggested by the reviewer. We re-attach the figures and tables with part of the modified text.**
  - 3) One of the most important critiques by the previous reviewer as well as myself is that your text is not argumentative. There are no reasons provided for why a certain marker or parameter for high tumor burden should or should not be included in the set of parameters through which high tumor burden is defined. There is no logical pretext for your definition and conclusions, merely a narrative summary of findings in other people's work. In other words, what is the justification for choosing "more than 3 metastatic sites, the sum of the longest diameters larger than 100 mm, metastatic liver involvement, multiple symptomatic brain involvement, and relevant functional patient deterioration" as criteria for HTB? This needs to be overly evident and premised in the preceding text. **We do consider that there are sufficient pretexts (exposed in the development of the manuscript) to conclude that the parameters mentioned could define HTB, since they are associated with a worse prognosis. It is true that the statistical quality of the studies presented is not mostly based on RCT, but there is very little published in this regard. However, we have added a sentence in the conclusions.**
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3<sup>rd</sup> Editorial decision  
29-Aug-2022

Ref.: Ms. No. JCTRes-D-22-00051R2  
High Tumor burden in non-small cell lung cancer. Review of the literature.  
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the  
Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly  
review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Comments from the editors and reviewers: